

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently amended) A method for the preparation of microspheres, which comprises the following circulation steps:

(a) emulsifying a medicament-containing polymer solution containing a medicament, a biocompatible and biodegradable hardly-water-soluble polymer and a water-immiscible organic solvent having a boiling point lower than that of water into an aqueous solution in an emulsifying device to form an emulsion wherein said medicament-containing polymer solution is dispersed in the aqueous solution;

(b) transferring the obtained emulsion into a microsphere storage tank;

(c) introducing a part of the emulsion from the microsphere storage tank into a cross flow filter;

(d-1)-i) returning a liquid passing over the cross flow filter to the microsphere storage tank;

(d-1)-ii) recycling a filtrate filtered from the ~~above~~ cross flow filter as an aqueous solution for step (a), repeating steps (a) to (d-1), and evaporating said water-immiscible organic solvent with a hollow fiber membrane module located in the microsphere storage tank during this circulation process; and

(e) collecting microspheres in the microsphere storage tank after step (d-1) is completed.

2. (Previously presented) The method according to claim 1, wherein the medicament-containing polymer solution is one of the following:

(i) a solution in which a biocompatible and biodegradable hardly-water-soluble polymer and a medicament are dissolved in a water-immiscible organic solvent having a boiling point lower than that of water;

(ii) a suspension in which a biocompatible and biodegradable hardly-water-soluble polymer is dissolved in a water-immiscible organic solvent having a boiling point lower than that of water, and a medicament is suspended in the resulting polymer solution;

(iii) a dispersion in which a biocompatible and biodegradable hardly-water-soluble polymer is dissolved in a water-immiscible organic solvent having a boiling point lower than that of water, and an aqueous solution of medicament is dispersed in the resulting polymer solution; and

(iv) a dispersion in which one of biocompatible and biodegradable hardly-water-soluble polymers is dissolved in a water-immiscible organic solvent having a boiling point lower than that of water, and a solution of the other biocompatible and biodegradable hardly-water-soluble polymer in the same organic solvent is dispersed in the resulting polymer solution, and further a medicament is dissolved or suspended in the dispersed polymer solution.

3 (Previously presented) The method according to claim 1, wherein the emulsification of step (a) is carried out continuously, and the resulting emulsion is transferred continuously into the microsphere storage tank.

4. (Previously presented) The method according to claim 1, wherein the emulsification of step (a) is carried out by batch-treatment, and the resulting emulsion in each batch is transferred individually into the microsphere storage tank.

5-6. (Cancelled).

7. (Currently amended) The method according to claim ~~[[6]]~~1, wherein the water-immiscible organic solvent having a boiling point lower than that of water is a halogenated aliphatic hydrocarbon solvent.

8-10. (Cancelled).

11. (Previously presented) The method according to claim 1, wherein during step (d-1), the filtration speed through the cross flow filter and the influx speed of the emulsion from the emulsifying device into the microsphere storage tank are controlled substantially the same so as to keep the volume of the emulsion in said tank substantially constant.

12. (Previously presented) The method according to claim 4, wherein the capacity of the microsphere storage tank is 10 to 1000 times of that of the emulsifying device for batch-treatment.

13. (Previously presented) The method according to claim 1, wherein the pore size of a membrane filter of the cross flow filter is in the range of 1/300 to 1/3 of the average particle size of the desired microspheres, and the filtration speed of the filtrate from the cross flow filter is adjusted to the range of 1/100 to 1/3 of the introduction speed of the emulsion into said cross flow filter.

14. (Original) The method according to claim 13, wherein the pore size of the membrane filter of the cross flow filter is within the range of 0.01 to 10 μm .

15. (Previously presented) The method according to claim 1, wherein the emulsifying step (a) is carried out with a high-speed rotary homogenizer utilizing inner shear (liquid-liquid shear).

16. (Previously presented) The method according to claim 1, wherein the emulsifying step (a) is carried out using the aqueous solution in a volume of 1 to 1000 times of that of the medicament-containing polymer solution.

17-18. (Cancelled).

19. (Previously presented) The method according to claim 1, wherein the biocompatible and biodegradable hardly-water-soluble polymer is a polyester of hydroxyfatty acid.

20. (Previously presented) The method according to claim 1, wherein the microspheres are collected by dead-end filtration, cross flow filtration or centrifugation, or a combination of these methods.

21. (Currently amended) The method according to claim 1, wherein the medicament is recovered from the aqueous solution after the collection of the microspheres.

22. (Previously presented) A method for preparation of lyophilized microspheres, which comprises preparing microspheres by the method as set forth in claim 1, dispersing the microspheres thus obtained in an aqueous solution of an excipient if necessary, and then subjecting the resultant to lyophilization.

23-31. (Cancelled).